We measured alveolar NO concentration, bronchial NO flux, and levels of 8-isoprostane and LTB_4 in exhaled breath condensate (EBC) in 61 subjects with COPD. These measurements were repeated in 40 patients after 4 weeks of treatment with inhaled fluticasone (500 μg b.i.d.).

Subjects with COPD had higher levels of 8-isoprostane and LTB_4 in EBC, increased alveolar NO concentration, but decreased bronchial NO flux as compared with healthy subjects. Bronchial NO flux correlated positively with β_2-agonist-induced change in FEV_1 (r=0.372, p=0.003), but other inflammatory markers were not related to lung function. Baseline levels of bronchial NO flux were associated with higher increase in FEV_1/FVC (r=0.313, p=0.049) and better symptom alleviation during the fluticasone treatment.

In conclusion, high bronchial NO flux in COPD predicts favourable acute response to β_2-agonists and a good response also to treatment with ICS. The other tested markers are not related to disease severity or treatment responses in COPD.

Hypoxia but not cigarette smoke modulates VEGF secretion from human T-cells

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Vascular endothelial growth factor (VEGF) is involved in lung development, angiogenesis and in response to injury. Chronic obstructive pulmonary disease (COPD) is an inflammatory disease characterised by accumulation of T-cells and remodelling of the airways. We hypothesized that T-cell secreted VEGF is modulated by cigarette-smoke and by a hypoxic microenvironment and that these conditions have an impact on protein secretion from T-cells from patients with COPD.

T-cells were isolated from peripheral blood of healthy donors and stimulated in normoxia and hypoxia with or without exposure to cigarette smoke extract (CE). VEGF and selected cytokines were measured in T-cell conditioned media (CBA flex set and ELISA). Hypoxia (1-2% O_2) stimulated VEGF secretion from T-cells, whereas the release of inflammatory cytokines (IL-4, IL-6, IL-10, IL-13, IFN-γ and TNF) were not affected. CE did not influence VEGF secretion neither in hypoxia nor in normoxia whereas cytokine secretion was inhibited by CE in both conditions. T-cells from COPD-patients (FEV_1 23-63 % of predicted) secreted significantly more VEGF compared to T-cells from age-matched healthy individuals.

The persistent VEGF secretion despite an inhibition of other T-cell secreted mediators by CE suggests that VEGF may act as a modulating factor in a hypoxic microenvironment in COPD. This hypothesis is supported by elevated VEGF levels from stimulated T-cells from COPD patients.

Small airway fibrosis in COPD: expression of procollagens I and III

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Type I and III collagen protein precursors are increased in fibrosing processes in the lung. The aim of this study was to compare the expression of these precursor proteins in the small airways of nonsmokers, smokers and COPD-patients with different severity of the disease, as a marker of newly formed fibrosis.

Procollagen I and III aminoterminal peptides (PINP and PIIINP) were studied by immunohistochemistry in lung tissue of 16 life-long non-smokers, 20 current smokers with normal lung function and 20 current smokers with COPD. Tissue specimens from tumor-free peripheral lung tissue were selected. COPD was defined according to GOLD criteria.

No expression of PINP was found in the subepithelial layer of small bronchioli. In peripheral bronchioli the PIIINP expressing layer was thickest in stage I-II COPD and thinnest in severe COPD (p=0.015). Western blotting of the total lung homogenates showed a higher level of PIIINP in nonsmokers compared to smoker groups.

In small airways, PIIINP expression increases in mild-moderate COPD but decreases at end-state disease, as a marker of cessation of active fibrogenesis. However, the total lung homogenate shows decreased expression of PIIINP in all smoker groups, referring to the possibility of balance shift towards degradation in other lung compartments.

Reference:
Kaarteenaho-Wiik R et al. Localization of precursor proteins and mRNA of type I and III collagens in usual interstitial pneumonia and sarcoidosis. J Mol Histol. 2005;36:437-46

Is COPD a risk factor for increased arterial stiffness?

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